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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/918,036	07/30/2001	Kiran Madura	266/165	1466
34055	7590	11/30/2005	EXAMINER	
PERKINS COIE LLP POST OFFICE BOX 1208 SEATTLE, WA 98111-1208			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/918,036

Applicant(s)

MADURA, KIRAN

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 September 2005.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 6,7,9,10 and 12 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☐ Claim(s) _____ is/are rejected.
7) ☒ Claim(s) 6,7,9,10 and 12 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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Reply under 37 CFR section 1.111 filed Sept 14, 2005 is acknowledged. Claims 1-5, 8, 11, and 13-18 were previously cancelled; claims 6 and 10 have been currently amended. Claims 6, 7, 9, 10 and 12 are pending and under examination.

DETAILED OFFICE ACTION

1. Rejections

1.1. 35 USC, section 112, first paragraph

1.1.1. Lack of written description

Rejection withdrawal

Rejection of claims 6, 7, 9, 10 and 12 made in the Office Action of June 17, 2005 (previous Action), for new matter, is withdrawn, because applicants canceled the term "functional 26S proteasome" which lack a definition in the disclosure.

Amended claims 6-7, 9, 10 and 12 are rejected because neither the specification nor the claims as originally filed define the term "catalytically active 26S proteasome". On page 6 of their current Remarks, Applicants turn the reader's attention their opinion, "the Applicant has established the correlation that 'a common biochemical property of a Ubl is its interaction with catalytically active 26S proteasome.' See page 42, lines 4-12 of the specification". The specification, indeed, comprises this phrase, however Applicants fail to define what the term "catalytically active 26S proteasome" means. There is also nothing to suggest in the specification, or the claims as originally filed, that Applicants limit their method to the cells with a catalytically active 26S proteasome. Introducing this limitation to the claims means introducing a new matter. Thus, the

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claims are rejected because they contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed a DNA construct for assessing whether any cell, i.e., all cells, not only yeast cells used by Inventors, having catalytically active 26S proteasome, is quiescent or actively growing. One skilled in the art realizes that yeast cells used by the inventors are not representative of all cells occurring in nature of man-engineered. The specification fails to provide a defining characteristic of catalytically active 26 proteasome". The term "catalytically active 26S proteasome" is generic because 26S proteasome is a very complex structure and there is no teaching which mutants of which components of the proteasome do not influence its catalytic activity and which do so. Applicants describe on page 2, line 30 and further, and on page 3, line 12 and further, the structure of 26S proteasome as an extremely complex structure. It consists of two subcomplexes, a catalytical one of 20S and a regulatory one of 19S. In line 20 on page 3 Applicants inform,

"The 19S complex contains as many as 20 subunits, which include a multiubiquitin-chain binding protein, isopeptidases and at least 6 ATPases. To date, many of these additional subunits remain uncharacterized."

Thus, the state of the art at the time of filing did not allowed for unequivocal definition of the term "catalytically active 26S proteasome".

In conclusion, because the Applicants did not reasonably convey to one skilled in the relevant art that at the time the application was filed they had possession of the claimed invention, the claims are rejected.

1.2.2. Scope of enablement

Claim 6-7 and 9, 10 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for degradation of Rad23¹⁻³⁶⁹, Rad23-HA and Ubl^{R23}-lacZ within 0-30 min. after labeling when the labeling is performed in some exponentially growing yeast transformants (Fig. 7 and 9), does not reasonably provide enablement for assessing whether a cell with a catalytically active 26S proteasome is quiescent or actively growing. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to a product and use of it for a method for assessing whether a cell (i.e. all cells) with a catalytically active 26S proteasome is quiescent or actively growing. The nature and breadth of the claimed invention encompasses using a DNA construct encoding for Ubl-reporter, wherein Ubl is any one of SEQ ID NO: 2-5 operably linked to any reporter, or any Ubl operably linked to reporter that is identified by claims 9 and 12 wherein said construct is transfected into a cell with a catalytically active 26S proteasome.

The art of transfection of DNA molecules into cells is highly developed and skills of artisan high, however, because Applicants do not define a catalytically active 26S

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proteasome, and for that matter a cell with a catalytically active 26S proteasome, one skilled in the art does not know which cell to choose as comprising "catalytically 26S proteasome" for transfection and assessment of the state of growth of the cell. Whether a cell has the catalytically active 26S proteasome is left to be determined by the one skilled in the art. This determination certainly involves an experimentation which is out of routine, taking into account the complexity of the 26 S proteasome structure and number of combination of mutations in the structure components that may/may not lead to degradation of the protein encoded by the claimed DNA construct.

The disclosure fails to provide guidance what a catalytically active 26S proteasome is, and in result, experimentation left to those in the art has low probability of success and is improperly extensive and undue. Although Applicants by the last amendment limited the claimed DNA construct to those tested in *S. cerevisiae*, their data does not enable the invention as broadly claimed, i.e. application to any cell having catalytically active proteasome. Without further teachings on the part of Applicants as to the cells comprising catalytically active 26S proteasome the experimentation imposed on the one skilled in the art is improperly extensive and undue.

Response to Applicant's arguments

In response to rejection under 35 USC section 112, first paragraph, Applicants argue,

"Applicant has disclosed illustrative examples of cells with a catalytically active 26S proteasome (e.g. wild type cells of the paragraph bridging pages 34 and 356) as

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well as lacking a catalytically active 26S proteasome (e.g., cim5-1 and pre-1 pre12-2 cells of the paragraph bridging pages 35 and 37). Given this guidance, one of skill would readily appreciate other types of cells which can be assessed in accordance with the instant method."

This argument is not persuasive for the following reasons. Even if one skilled in the art assumes that wild type yeast cells possess "catalytically active proteasome" these cells are not representative of all cells possessing "catalytically active proteasome" broadly claimed in the method and function of the product i.e. DNA. Yeast cells are not representative of all cells existing naturally or engineered by man. There is no guidance which cells (i.e. which mutants are to be excluded or included from the scope of the claimed method. Applicants do not disclose human and other species homologs of yeast cim5-1 and pre-1 and pre2-2 mutants. And finally, and the most importantly, Applicant's primary intention is "to assess the proliferative potential of tumor cells", page 5 line 19 of the specification. However, on page 2 line 24 Applicant states,

"It is clear that defects in the functioning of the ubiquitin/proteasome system can have severe consequences on biological homeostasis. Indeed, mutation that affect the degradation of many protein listed above have been associated with tumorigenesis."

Thus, Applicant admits that tumorigenesis is related to lack of normal catalytically active 26S proteasome, i.e. cells of many tumor cells do not have "a wild type of 26S proteasome". Therefore, the proposed method cannot be used for cells to be expected

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being tumor, or tumor cells, to assess whether they are quiescent or actively growing. Thus the method claimed cannot be used in the most important intended application.

In summary, the claims remain rejected for the reasons explained in paragraphs 1.1.1. and 1.1.2 above and in response to Applicants' arguments.

3. Conclusion

All claims remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the

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examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent Examiner


PONNATHAPU ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600